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USPT,PGPB	(l16 or l15 or l14 or l13 or l12 or l11 or l10) and l8 and l6 and l1	3	L17
USPT,PGPB	(((435/938)!.CCLS.))	100	L16
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USPT,PGPB	((435/136)!.CCLS.)	329	L10
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USPT,PGPB	Hydroxylation or alkane$1	33596	L5
USPT,PGPB	l2 and l1	52	L4
USPT,PGPB	pichia pastoris	972	L3
USPT,PGPB	candida maltosa or Candida cloacae or Candida novellus or Candida subtropicalis	177	L2
USPT,PGPB	dicarboxylic acid$1 or Carboxylic acid$1 or monocarboxylic acid$1	155036	L1

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☐ 1. Document ID: US 6020288 A

L7: Entry 1 of 2 File: USPT Feb 1, 2000

US-PAT-NO: 6020288
DOCUMENT-IDENTIFIER: US 6020288 A

TITLE: Methods and compositions for enhancing cytochrome P450 in plants

DATE-ISSUED: February 1, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nonomura; Arthur M.	Boxborough	MA	01719	N/A
Benson; Andrew A.	La Jolla	CA	92037	N/A
Nishio; John N.	Laramie	WY	82070-3917	N/A

APPL-NO: 8/ 927415
DATE FILED: September 11, 1997

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent application Ser. No. 08/610,928, filed Mar. 5, 1996, now U.S. Pat. No. 5,846,908, which is a continuation-in part of U.S. patent application Ser. No. 08/399,399, filed Mar. 6, 1995; which was a continuation-in part of Ser. No. 08/351,348 filed Dec. 9, 1994, now U.S. Pat. No. 5,597,400 issued on Jan. 28, 1997, which was a continuation-in-part of U.S. patent application Ser. No. 07/901,366, filed on Jun. 19, 1992. The full disclosures of each of these patent applications are incorporated herein by reference. Related international application are PCT/US96/02444 (equivalent of Ser. No. 08/610,928) and PCT/US93/05676 (equivalent of Ser. No. 08/351,348).

INT-CL: [6] A01N 31/00, A01N 37/00, A01N 43/22, A01N 57/02
US-CL-ISSUED: 504/127; 504/128, 504/130, 504/136, 504/138, 504/140, 504/142, 504/143, 504/144, 504/149
US-CL-CURRENT: 504/127; 504/128, 504/130, 504/136, 504/138, 504/140, 504/142, 504/143, 504/144, 504/149
FIELD-OF-SEARCH: 504/127, 504/128, 504/130, 504/136, 504/138, 504/140, 504/142, 504/143, 504/144, 504/149

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
3897241	July 1975	Washio et al.	71/113
4799953	January 1989	Danzig et al.	71/98
4846877	July 1989	Azuma et al.	71/92
5298482	March 1994	Tanaka et al.	504/320
5300540	April 1994	Masters	523/309
5532204	July 1996	Joshi	504/118
5597400	January 1997	Nonomura et al.	71/28

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
0 465 907 A1	January 1992	EPX	
2689905	October 1993	FRX	
2004856	April 1979	GBX	

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ART-UNIT: 166
PRIMARY-EXAMINER: Clardy; S. Mark
ATTY-AGENT-FIRM: Nields, Lemack & Dingman

ABSTRACT:

The present invention provides methods for treating plants which comprise application of an oxidant that induces NADPH:cytochrome P450 reductase and application of a reductant that induces cytochrome P450 monooxygenase. The present invention also provides methods for increasing cytochrome P450 in plants and for enhancing the growth of plants. The present invention also provides compositions and systems useful in the methods of the present invention.

38 Claims, 1 Drawing figures

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 2. Document ID: US 5254466 A

L7: Entry 2 of 2 File: USPT Oct 19, 1993

US-PAT-NO: 5254466
DOCUMENT-IDENTIFIER: US 5254466 A

TITLE: Site-specific modification of the candida tropicals genome

DATE-ISSUED: October 19, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Picataggio; Stephen	Santa Rosa	CA	N/A	N/A
Deanda; Kristine	Graton	CA	N/A	N/A
Eirich; L. Dudley	Santa Rosa	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Henkel Research Corporation	Santa Rosa	CA	N/A	N/A	02

APPL-NO: 7/ 432091

DATE FILED: November 6, 1989

INT-CL: [5] C12N 15/09, C12P 7/44
US-CL-ISSUED: 435/142; 435/172.1, 435/172.3, 435/924, 435/254.22
US-CL-CURRENT: 435/142; 435/254.22, 435/477, 435/481, 435/483, 435/484, 435/490, 435/6, 435/924
FIELD-OF-SEARCH: 435/67.1, 435/142, 435/172.3, 435/172.1, 435/940, 435/255, 435/924, 935/22, 935/28

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
4735901	April 1988	Kurtz et al.	435/172.3

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
183070	April 1986	EPX	

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Proceeding National Academy of Science, vol. 76 No. 10 issued Oct. 1979. S. Scherer et al. "Replacement of Chromosome Segments with altered DNA sequences constructed in vitro". pp. 4951-4955.

ART-UNIT: 185
PRIMARY-EXAMINER: Schwartz; Richard A.
ASSISTANT-EXAMINER: LeGuyader; J.
ATTY-AGENT-FIRM: Szoke; Ernest G. Jaeschke; Wayne C. Drach; John E.

ABSTRACT:

The POX genes of C. tropicalis are disrupted resulting in the complete blockage of the beta-oxidation pathway in the strain. Fermentation of C. tropicalis cells having disrupted genes on alkane, fatty acid and fatty acid ester substrates produces substantially pure dicarboxylic acids in substantially quantitative yield.

30 Claims, 5 Drawing figures

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Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. Document ID: US 6020288 A

L9: Entry 1 of 2 File: USPT Feb 1, 2000

US-PAT-NO: 6020288
DOCUMENT-IDENTIFIER: US 6020288 A

TITLE: Methods and compositions for enhancing cytochrome P450 in plants

DATE-ISSUED: February 1, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nonomura; Arthur M.	Boxborough	MA	01719	N/A
Benson; Andrew A.	La Jolla	CA	92037	N/A
Nishio; John N.	Laramie	WY	82070-3917	N/A

US-CL-CURRENT: 504/127; 504/128, 504/130, 504/136, 504/138, 504/140, 504/142, 504/143, 504/144, 504/149

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 5254466 A

L9: Entry 2 of 2 File: USPT Oct 19, 1993

US-PAT-NO: 5254466
DOCUMENT-IDENTIFIER: US 5254466 A

TITLE: Site-specific modification of the candida tropicals genome

DATE-ISSUED: October 19, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Picataggio; Stephen	Santa Rosa	CA	N/A	N/A
Deanda; Kristine	Graton	CA	N/A	N/A
Eirich; L. Dudley	Santa Rosa	CA	N/A	N/A

US-CL-CURRENT: 435/142; 435/254.22, 435/477, 435/481, 435/483, 435/484, 435/490, 435/6, 435/924

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. Document ID: US 6174673 B1

L17: Entry 1 of 3 File: USPT Jan 16, 2001

US-PAT-NO: 6174673
DOCUMENT-IDENTIFIER: US 6174673 B1

TITLE: High throughput screening for novel enzymes

DATE-ISSUED: January 16, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A
Keller; Martin	San Diego	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Diversa Corporation	San Diego	CA	N/A	N/A	02

APPL-NO: 9/ 098206
DATE FILED: June 16, 1998

PARENT-CASE:
This application is a continuation-in-part of U.S. application Ser. No. 08/876,276, filed Jun. 16, 1997.

INT-CL: [7] C12Q 1/68
US-CL-ISSUED: 435/6; 435/69.1, 435/440, 435/471, 435/476, 435/320.1
US-CL-CURRENT: 435/6; 435/320.1, 435/440, 435/471, 435/476, 435/69.1
FIELD-OF-SEARCH: 435/6, 435/69.1, 435/440, 435/320.1, 435/471, 435/476

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
4399219	August 1983	Weaver	435/34
4643968	February 1987	Weaver	435/32
4647536	March 1987	Mosbach et al.	435/177
4916060	April 1990	Weaver	435/29
4959301	September 1990	Weaver et al.	435/5
5055390	October 1991	Weaver et al.	435/5
5225332	July 1993	Weaver et al.	435/29
5824485	October 1998	Thompson et al.	435/6

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
WO 98/56904	December 1998	WOX	
WO 99/49315	September 1999	WOX	
WO99/54494	October 1999	WOX	

OTHER PUBLICATIONS

Zhang et al. FASEB J. vol. 5, pp. 3108-3113, 1991.
Plovins et al. Applied and Environmental Microbiology. vol. 60(12), pp. 4638-4641, 1994.

ART-UNIT: 166
PRIMARY-EXAMINER: Yucel; Remy
ATTY-AGENT-FIRM: Gray Gary Ware & Freidenrich LLP Haile; Lisa A.

ABSTRACT:

Disclosed is a process for identifying clones having a specified activity of interest, which process comprises (i) generating one or more expression libraries derived from nuclei acid directly isolated from the environment; and (ii) screening said libraries utilizing a fluorescence activated cell sorter to identify said clones. More particularly, this is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) exposing said libraries to a particular substrate or substrates of interest; and (iii) screening said exposed libraries utilizing a fluorescence activated cell sorter to identify clones which react with the substrate or substrates. Also provided is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; and (ii) screening said exposed libraries utilizing an assay requiring co-encapsulation, a binding event or the covalent modification of a target, and a fluorescence activated cell sorter to identify positive clones.

23 Claims, 18 Drawing figures

☐ 2. Document ID: US 6168919 B1

L17: Entry 2 of 3 File: USPT Jan 2, 2001

US-PAT-NO: 6168919
DOCUMENT-IDENTIFIER: US 6168919 B1

TITLE: Screening methods for enzymes and enzyme kits

DATE-ISSUED: January 2, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Diversa Corporation	San Diego	CA	N/A	N/A	02

APPL-NO: 8/ 983367
DATE FILED: September 30, 1998

PCT-DATA:

APPL-NO	DATE-FILED	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
PCT/US96/11854	July 17, 1996	WO97/04077	Feb 6, 1997	Sep 30, 1998	Sep 30, 1998

INT-CL: [7] C12Q 1/68, C12Q 1/00, C12P 19/34, C12N 15/64
US-CL-ISSUED: 435/6; 435/4, 435/91.1, 435/91.4, 435/91.41, 435/252.3, 435/183, 435/320.1, 435/325, 536/23.1, 536/23.2, 536/23.4
US-CL-CURRENT: 435/6; 435/183, 435/252.3, 435/320.1, 435/325, 435/4, 435/91.1, 435/91.4, 435/91.41, 536/23.1, 536/23.2, 536/23.4
FIELD-OF-SEARCH: 435/4, 435/6, 435/91.1, 435/91.4, 435/91.41, 435/252.3, 435/183, 435/320.1, 435/325, 536/23.1, 536/23.2, 536/23.4

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
5171684	December 1992	Yen et al.	435/252.3
5712146	January 1998	Khosla et al.	435/252.35
5958672	September 1999	Short	435/4

OTHER PUBLICATIONS

Lactic Dehydrogenase, Sigma catalog, p. 634, 1997.
Anderson et al., Met. Enzymol., vol. 68, pp. 428-436, 1979.
Promega Catalog, p. 205, 1993.
Sambrook et al., Molecular Cloning, Cold Spring Harbor Laboratory Press, vol. 2, p. 9.30 and pp. 12.1-12.20, 1989.*

ART-UNIT: 162
PRIMARY-EXAMINER: Achutamurthy; Ponnathapu
ASSISTANT-EXAMINER: Tung; Peter P.
ATTY-AGENT-FIRM: Gray, Cary, Ware & Freidenrich LLP Haile; Lisa A.

ABSTRACT:

Recombinant enzyme libraries and kits where a plurality of enzymes are each characterized by different physical and/or chemical characteristics and classified by common characteristics. The characteristics are determined by screening of recombinant enzymes expressed by a DNA library produced from various microorganisms. Also disclosed is a process for identifying clones of a recombinant library which express a protein with a desired ctivity by screening a library of expression clones randomly produced from DNA of at least one microorganism, said screeing being effected on expression products of said clones to thereby identify clones which express a protein with a desired activity. Also disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein activity by screening for a specified protein activity in a library of clones prepared by (I) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein activity.

9 Claims, 8 Drawing figures

☐ 3. Document ID: US 5254466 A

L17: Entry 3 of 3 File: USPT Oct 19, 1993

US-PAT-NO: 5254466
DOCUMENT-IDENTIFIER: US 5254466 A

TITLE: Site-specific modification of the candida tropicals genome

DATE-ISSUED: October 19, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Picataggio; Stephen	Santa Rosa	CA	N/A	N/A
Deanda; Kristine	Graton	CA	N/A	N/A
Eirich; L. Dudley	Santa Rosa	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Henkel Research Corporation	Santa Rosa	CA	N/A	N/A	02

APPL-NO: 7/ 432091
DATE FILED: November 6, 1989

INT-CL: [5] C12N 15/09, C12P 7/44
US-CL-ISSUED: 435/142; 435/172.1, 435/172.3, 435/924, 435/254.22
US-CL-CURRENT: 435/142; 435/254.22, 435/477, 435/481, 435/483, 435/484, 435/490, 435/6, 435/924
FIELD-OF-SEARCH: 435/67.1, 435/142, 435/172.3, 435/172.1, 435/940, 435/255, 435/924, 935/22, 935/28

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
4735901	April 1988	Kurtz et al.	435/172.3

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
183070	April 1986	EPX	

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"Journal of Cell Biology., vol. 105 issued Jul. 1987., T. M. Small et al. "Export of the carboxy-terminal Portion of Acyl-CoA oxidase into Peroxisomes of Candida tropicalis" pp. 217-252.
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Gene vol. 51, issued 1987, W. W. Murray et al, "The primary structure of a peroxisomal fatty acyl-CoA oxidase from the yeast Canada tropicalis p K233", pp. 119-128.
Proceeding National Academy of Science, vol. 76 No. 10 issued Oct. 1979. S. Scherer et al. "Replacement of Chromosome Segments with altered DNA sequences constructed in vitro". pp. 4951-4955.

ART-UNIT: 185
PRIMARY-EXAMINER: Schwartz; Richard A.
ASSISTANT-EXAMINER: LeGuyader; J.
ATTY-AGENT-FIRM: Szoke; Ernest G. Jaeschke; Wayne C. Drach; John E.

ABSTRACT:

The POX genes of C. tropicalis are disrupted resulting in the complete blockage of the beta-oxidation pathway in the strain. Fermentation of C. tropicalis cells having disrupted genes on alkane, fatty acid and fatty acid ester substrates produces substantially pure dicarboxylic acids in substantially quantitative yield.

30 Claims, 5 Drawing figures

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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L2             1 SEA ABB=ON  PLU=ON  9038-14-6/RN
                 D
L3             1 SEA ABB=ON  PLU=ON  9023-03-4/RN
                 D

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L4               SEL PLU=ON  L2 1- CHEM :      26 TERMS
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L5               SEL PLU=ON  L3 1- CHEM :      16 TERMS
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L7          7478 SEA ABB=ON  PLU=ON  L5
L8          1165 SEA ABB=ON  PLU=ON  L6 AND L7
L9        188643 SEA ABB=ON  PLU=ON  DICARBOXYLIC ACID# OR (CARBOXYLIC ACIDS
                 (L) DICARBOXYLIC) OR CARBOXYLIC ACID# OR MONOCARBOXYLIC ACID#
L10            0 SEA ABB=ON  PLU=ON  L8 (L) L9
L11         5883 SEA ABB=ON  PLU=ON  (HYDROXYLATION (L) .OMEGA.-HYDROXYLATION)
                 OR (HYDROXYLATION (L) ALKANE#) OR (.ALPHA.-HYDROXYLATION) OR
                 (HYDROXYLATION (L) .ALPHA.)
L12            0 SEA ABB=ON  PLU=ON  L9 AND L10
L13          149 SEA ABB=ON  PLU=ON  L9 AND L11
L14            8 SEA ABB=ON  PLU=ON  L13 AND (L6 OR L7)
L15            8 DUP REM L14 (0 DUPLICATES REMOVED)
                 D IBIB AB 1-8
                 D IBIB AB HIT 1-8
L16            8 SEA L15
L17            5 SEA ABB=ON  PLU=ON  L16 AND (PREP/RL OR PREPAR? OR SYNTH? OR
                 MAK?)
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L17 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:133824 CAPLUS
DOCUMENT NUMBER: 132:162018
TITLE: DNA shuffling of **monooxygenase** genes for production of industrial chemicals
INVENTOR(S): Affholter, Joseph A.; Davis, Christopher; Selifonov, Sergey A.
PATENT ASSIGNEE(S): Maxygen, Inc., USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009682	A1	20000224	WO 1999-US18424	19990812
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9953479	A1	20000306	AU 1999-53479	19990812

PRIORITY APPLN. INFO.: US 1998-96271 P 19980812
US 1999-130810 P 19990423
WO 1999-US18424 W 19990812

OTHER SOURCE(S): MARPAT 132:162018

AB This invention provides improved **monooxygenases**, dehydrogenases, and transferases that are useful for the biocatalytic **synthesis** of compds. such as .alpha.-hydroxycarboxylic acids, and aryl- and alkyl-, hydroxy compds. The polypeptides provided herein are improved in properties such as regioselectivity, enzymic activity, stereospecificity, and the like. Methods for obtaining recombinant polynucleotides that encode these improved polypeptides are also provided, as are organisms that express the polypeptides and are thus useful for carrying out said biocatalytic **syntheses**. In the methods for obtaining **monooxygenase** genes, a plurality of parental forms (homologs) of a selected nucleic acid are recombined. The selected nucleic acid derived either from one or more parental nucleic acid(s) which encodes a **monooxygenase** enzyme, or a fragment thereof, or from a parental nucleic acid which does not encode **monooxygenase**, but which is a candidate for DNA shuffling to develop **monooxygenase** activity. The plurality of forms of the selected nucleic acid differ from each other in at lease one (and typically two or more) nucleotides, and, upon recombination, provide a library of recombinant **monooxygenase** nucleic acids. The library can be an in vitro set of mols., or present in cells, phage or the like. The library is screened to identity at least one recombinant **monooxygenase** nucleic acid that exhibits distinct or improved **monooxygenase** activity compared to the parental nucleic acid or nucleic acids. Also provided by the invention

are methods for increasing said solvent resistance of organisms that are used in the **synthetic** methods.

REFERENCE COUNT: 18

REFERENCE(S):
(1) Affymax Tech Nv; WO 9720078 A 1997 CAPLUS
(2) Agency Of Ind Sci & Technology; JP 05-049474 A 1993 CAPLUS
(3) Aoyama, T; JOURNAL OF BIOLOGICAL CHEMISTRY 1989, V264(18), P10388 CAPLUS
(4) Crameri, A; NATURE 1998, V391, P288 CAPLUS
(5) Dierks, E; THE JOURNAL OF BIOLOGICAL CHEMISTRY 1998, V273(36), P23055 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI DNA shuffling of **monooxygenase** genes for production of industrial chemicals

AB This invention provides improved **monooxygenases**, dehydrogenases, and transferases that are useful for the biocatalytic **synthesis** of compds. such as .alpha.-hydroxycarboxylic acids, and aryl- and alkyl-, hydroxy compds. The polypeptides provided herein are improved in properties such as regioselectivity, enzymic activity, stereospecificity, and the like. Methods for obtaining recombinant polynucleotides that encode these improved polypeptides are also provided, as are organisms that express the polypeptides and are thus useful for carrying out said biocatalytic **syntheses**. In the methods for obtaining **monooxygenase** genes, a plurality of parental forms (homologs) of a selected nucleic acid are recombined. The selected nucleic acid derived either from one or more parental nucleic acid(s) which encodes a **monooxygenase** enzyme, or a fragment thereof, or from a parental nucleic acid which does not encode **monooxygenase**, but which is a candidate for DNA shuffling to develop **monooxygenase** activity. The plurality of forms of the selected nucleic acid differ from each other in at lease one (and typically two or more) nucleotides, and, upon recombination, provide a library of recombinant **monooxygenase** nucleic acids. The library can be an in vitro set of mols., or present in cells, phage or the like. The library is screened to identity at least one recombinant **monooxygenase** nucleic acid that exhibits distinct or improved **monooxygenase** activity compared to the parental nucleic acid or nucleic acids. Also provided by the invention are methods for increasing said solvent resistance of organisms that are used in the **synthetic** methods.

ST **monooxygenase** industrial **synthesis** DNA shuffling gene

IT Bioreactors
Nucleic acid library
Phage display library
Recombination, genetic
Regiochemistry
(DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Gene
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Amines, biological studies
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(N-dealkylation; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Ethers, biological studies

RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(O-dealkylation; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Thiols (organic), biological studies
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(S-dealkylation; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Ethers, biological studies
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(allyl, substrate; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Baeyer-Villiger oxidation
Dealkylation
Decarboxylation
Dehalogenation
Dehydrogenation
Epoxidation
Hydroxylation
Oxidation
(enzymic; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Alkenes, biological studies
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(epoxidn.; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Aromatic hydrocarbons, biological studies
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(halo, oxidative dehalogenation; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT **Carboxylic acids**, biological studies
RL: BPN (Biosynthetic preparation); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**
(hydroxy, conversion from olefins; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT **Alkanes**, biological studies
Aromatic hydrocarbons, biological studies
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(**hydroxylation**; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Chemicals
(industrial; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Solvents
(org., resistance to; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Sulfonylureas
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(oxygenation; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BIOL (Biological study); **PREP (Preparation)**

(solvent-resistant; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT Glycols, biological studies
RL: BPN (Biosynthetic preparation); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**
(vicinal, conversion from olefins; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 9003-99-0P, Peroxidase 9013-18-7P, Acyl-CoA Ligase 9023-26-1P, Coenzyme A transferase 9024-04-8P, Mandelate racemase 9031-56-5P, Ligase 9033-07-2P, Glycosyltransferase 9033-25-4P, Methyltransferase 9035-51-2P, Cytochrome P 450, **preparation** 9035-82-9P, Dehydrogenase **9038-14-6P**, **Monooxygenase** 9047-61-4P, Transferase 9048-63-9P, Epoxide hydrolase 9054-54-0P, Acyltransferase 9080-22-2P, Racemase 102055-73-2P, Oxo acid decarboxylase
RL: BPN (Biosynthetic preparation); CAT (Catalyst use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 60-12-8DP, 2-Phenylethanol, substituted 60-12-8P, 2-Phenylethanol 100-51-6DP, Benzyl alcohol, substituted 100-51-6P, Benzyl alcohol, biological studies 122-97-4DP, 3-Phenylpropanol, substituted 122-97-4P, 3-Phenylpropanol
RL: BPN (Biosynthetic preparation); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**
(DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 145-13-1P, Pregnenolone
RL: BPN (Biosynthetic preparation); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**
(conversion from cholesterol; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 81093-37-0P, Pravastatin
RL: BPN (Biosynthetic preparation); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**
(conversion from mevastatin; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(conversion to pregnenolone; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 119-84-6, 3,4-Dihydrocoumarin 73573-88-3, Mevastatin
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(hydroxylation; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 59865-13-3, Cyclosporin 79217-60-0, Cyclosporin
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(modification; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

IT 78-79-5, Isoprene, biological studies 100-42-5, Styrene, biological studies 106-99-0, Butadiene, biological studies 107-02-8, Acrolein, biological studies 557-40-4, Diallyl ether 1321-74-0, Divinylbenzene, biological studies 1321-74-0D, Divinylbenzene, substituted 1746-13-0, Allyl phenyl ether 1746-13-0D, Allyl phenyl ether, substituted

25168-07-4, Vinylcyclohexene 40356-67-0, Vinylnorbornene
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(substrate; DNA shuffling of **monooxygenase** genes for prodn. of industrial chems.)

L17 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:77701 CAPLUS
DOCUMENT NUMBER: 130:138397
TITLE: Yeasts with elevated cytochrome P450 levels and their use in the manufacture of monoterminal and diterminal aliphatic carboxylates from alkanes
INVENTOR(S): Fallon, Robert D.; Payne, Mark S.; Picataggio, Stephen K.; Wu, Shijun
PATENT ASSIGNEE(S): E.I. Du Pont De Nemours and Company, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9904014	A2	19990128	WO 1998-US14935	19980720
WO 9904014	A3	19990520		
W: AU, CA, IL, JP, NZ, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9884982	A1	19990210	AU 1998-84982	19980720
EP 1003881	A2	20000531	EP 1998-935806	19980720
R: DE, DK, ES, FR, GB, IT, NL, SE, IE				

PRIORITY APPLN. INFO.: US 1997-53215 P 19970721
WO 1998-US14935 W 19980720

AB Strains of Pichia pastoris and Candida maltosa that have increased cytochrome P 450 activity or lack the .beta.-oxidn. pathway that can be used to convert c6-C22 alkanes to monoterminal and diterminal **carboxylic acids** are described. Expression constructs carrying cytochrome P 450 genes under the control of powerful inducible promoters (AOX1, PGK) were constructed by std. methods and introduced into P. pastoris or C. maltosa to give novel or increased P 450 activities. Disruption of .beta.-oxidn. in C. maltosa was achieved by insertional inactivation of the POX4 gene. A strain of C. maltosa cultured in a complete medium that was supplemented with dodecane 20 g/L when glucose was almost completely depleted was able to generate dodecanedioic acid at 3.4 g/h for 51 h.

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3.4 g/h for 51 h.

ST Pichia **alkane hydroxylation** carboxylic **dicarboxylic acid** manuf; cytochrome P450 Candida Pichia **alkane carboxylic acid** fermn; Candida **alkane hydroxylation** carboxylic **dicarboxylic acid** manuf

IT **Carboxylic acids, preparation**
Dicarboxylic acids
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); **PREP (Preparation)**
(C6-22; yeasts with elevated cytochrome P 450 levels and their use in manuf. of monoterminal and diterminal aliph. carboxylates from alkanes)

IT Fermentation
(**carboxylic acids**, with transgenic yeasts; yeasts with elevated cytochrome P 450 levels and their use in manuf. of monoterminal and diterminal aliph. carboxylates from alkanes)

IT Plasmid vectors
(pLPA1T, alkane **monooxygenase** gene on, expression in Pichia of; yeasts with elevated cytochrome P 450 levels and their use in manuf. of monoterminal and diterminal aliph. carboxylates from alkanes)

IT Plasmid vectors
(pSW84, alkane **monooxygenase** and cytochrome reductase genes on, expression in Candida of; yeasts with elevated cytochrome P 450 levels and their use in manuf. of monoterminal and diterminal aliph. carboxylates from alkanes)

IT Plasmid vectors
(pSW87, alkane **monooxygenase** and cytochrome reductase genes on, expression in Candida of; yeasts with elevated cytochrome P 450 levels and their use in manuf. of monoterminal and diterminal aliph. carboxylates from alkanes)

IT **9038-14-6, Monooxygenase** 9059-16-9, Alkane **monooxygenase** 106178-16-9, Fatty acid **monooxygenase**
RL: BPR (Biological process); BUU (Biological use, unclassified); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(in alkane utilization by yeasts; yeasts with elevated cytochrome P 450 levels and their use in manuf. of monoterminal and diterminal aliph. carboxylates from alkanes)

IT 693-23-2P, Dodecanedioic acid
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); **PREP (Preparation)**
(manuf. from dodecane of; yeasts with elevated cytochrome P 450 levels and their use in manuf. of monoterminal and diterminal aliph. carboxylates from alkanes)

L17 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1993:5685 CAPLUS
DOCUMENT NUMBER: 118:5685
TITLE: Metabolic engineering of Candida tropicalis for the production of long-chain **dicarboxylic acids**
AUTHOR(S): Picataggio, Stephen; Rohrer, Tracy; Deanda, Kristine; Lanning, Dawn; Reynolds, Robert; Mielenz, Jonathan; Eirich, L. Dudley
CORPORATE SOURCE: Microb. Technol. Dep., Cognis Inc., Santa Rosa, CA, 95407, USA
SOURCE: Bio/Technology (1992), 10(8), 894-8
CODEN: BTCHDA; ISSN: 0733-222X

DOCUMENT TYPE: Journal
LANGUAGE: English

AB An industrial strain of the yeast C. tropicalis was engineered for the efficient prodn. of long-chain **dicarboxylic acids**, which are important raw materials for the chem. industry. By sequential disruption of the 4 genes encoding both isoenzymes of the acyl-CoA oxidase which catalyzes the first reaction in the .beta.-oxidn. pathway, **alkane** and fatty acid substrates were successfully redirected to the .omega.-oxidn. pathway. Consequently, the conversion efficiency and chem. selectivity of their terminal oxidn. to the corresponding **dicarboxylic acids** was improved to 100%. The specific productivity of the bioconversion was increased further by amplification of the **cytochrome P 450** **monooxygenase** and NADPH-cytochrome reductase genes encoding the rate-limiting .omega.-hydroxylase in the .omega.-oxidn. pathway. The amplified strains demonstrated increased .omega.-hydroxylase activity and a 30% increase in productivity compared to the .beta.-oxidn.-blocked strain in fermns. The bioconversion is effective for the selective terminal oxidn. of both satd. and unsatd. linear aliph. substrates with C12-22 chain-lengths and also avoids the undesirable chain modifications assocd. with passage through the .beta.-oxidn. pathway, such as unsatn., **hydroxylation**, or chain shortening. It is now possible to efficiently produce a wide range of previously unavailable satd. and unsatd. **dicarboxylic acids** with a high degree of purity.

TI Metabolic engineering of Candida tropicalis for the production of long-chain **dicarboxylic acids**

AB An industrial strain of the yeast C. tropicalis was engineered for the efficient prodn. of long-chain **dicarboxylic acids**, which are important raw materials for the chem. industry. By sequential disruption of the 4 genes encoding both isoenzymes of the acyl-CoA oxidase which catalyzes the first reaction in the .beta.-oxidn. pathway, **alkane** and fatty acid substrates were successfully redirected to the .omega.-oxidn. pathway. Consequently, the conversion efficiency and chem. selectivity of their terminal oxidn. to the corresponding **dicarboxylic acids** was improved to 100%. The specific productivity of the bioconversion was increased further by amplification of the **cytochrome P 450** **monooxygenase** and NADPH-cytochrome reductase genes encoding the rate-limiting .omega.-hydroxylase in the .omega.-oxidn. pathway. The amplified strains demonstrated increased .omega.-hydroxylase activity and a 30% increase in productivity compared to the .beta.-oxidn.-blocked strain in fermns. The bioconversion is effective for the selective terminal oxidn. of both satd. and unsatd. linear aliph. substrates with C12-22 chain-lengths and also avoids the undesirable chain modifications assocd. with passage through the .beta.-oxidn. pathway, such as unsatn., **hydroxylation**, or chain shortening. It is now possible to efficiently produce a wide range of previously unavailable satd. and unsatd. **dicarboxylic acids** with a high degree of purity.

ST genetic engineering Candida **dicarboxylic acid** prodn

IT Candida tropicalis
(genetic engineering of, for long-chain **dicarboxylic acid** prodn.)

IT Genetic engineering
(of Candida tropicalis, for long-chain **dicarboxylic acid** prodn.)

IT **Carboxylic acids, preparation**

RL: **PREP (Preparation)**
(di-, long-chain, manuf. of, genetic engineering of Candida tropicalis for)

L17 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:61628 CAPLUS
DOCUMENT NUMBER: 102:61628
TITLE: Oxidative ether cleavage with p-nitroperbenzoic acid
AUTHOR(S): Schneider, Hans Joerg; Ahlhelm, Alfred; Mueller, Walter
CORPORATE SOURCE: Univ. Saarlandes, Saarbruecken, D-6600/11, Fed. Rep. Ger.
SOURCE: Chem. Ber. (1984), 117(11), 3297-302
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The reaction of p-nitroperbenzoic acid in CHCl3 with Me2CH(CH2)3OMe and (Me2CHCH2CH2)2O leads by selective attack at C-H bonds in the . **alpha**.-position to the ether oxygen to hemiacetals, which decomp. to aldehydes and alcs., yielding **carboxylic acids**. Secondary alkoxy groups, as in ethoxycyclohexane, furnish Baeyer-Villiger oxidn. products of initially formed ketones. Kinetic measurements with substituted benzyl Me ethers show a Hammett reaction const. .rho. = -0.9, which is in accord with the obsd. relatively small discrimination between secondary and tertiary C-H bonds. The results are compared with similar **hydroxylations** of **alkanes** and with **monooxygenase** reactions and point to oxenoid transition states. Radical reactions, as found with some **alkanes** are not obsd., which is shown by the small amts. of PhNO2 (.ltoreq.10%) formed during the reaction. 13C-NMR shifts of several ethers and oxidn. products are reported.

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IT 123-51-3P 502-44-3P 503-74-2P 622-45-7P 626-89-1P 646-07-1P 2412-73-9P 5299-60-5P 94368-15-7P 94368-16-8P
RL: **PREP (Preparation)**
(formation and carbon-13 NMR of)

L17 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1977:498893 CAPLUS
DOCUMENT NUMBER: 87:98893
TITLE: Biosynthesis of cutin. **.omega.**-**Hydroxylation** of fatty acids by a microsomal **preparation** from germinating Vicia faba
AUTHOR(S): Soliday, Charles L.; Kolattukudy, P. E.
CORPORATE SOURCE: Dep. Agric. Chem., Washington State Univ., Pullman, Wash., USA
SOURCE: Plant Physiol. (1977), 59(6), 1116-21
CODEN: PLPHAY

DOCUMENT TYPE: Journal
LANGUAGE: English

AB .omega.-**Hydroxylation** of fatty acids, which is a key reaction in the biosynthesis of cutin and suberin, was demonstrated in a cell-free **prepn**. from a higher plant. A crude microsomal fraction (105,000-g pellet) from germinating embryonic shoots of V. faba catalyzed the conversion of palmitic acid to .omega.-hydroxypalmitic acid.

As the crude cell-free **prepn**. also catalyzes the formation of other hydroxy acids such as .**alpha**.- and .beta.-hydroxy acids, the .**omega**.-**hydroxylation** product was identified by gas chromatog. on a polyester column and reverse phase, high performance liq. chromatog., 2 techniques which were shown to resolve the positional isomers. Gas chromatog. anal. of the **dicarboxylic acid** obtained by CrO3 oxidn. of the enzymic product also confirmed the identity of the enzymic .**omega**.-**hydroxylation** product. This enzymic **hydroxylation** required O and NADPH, but substitution of NADH resulted in nearly half the reaction rate obtained with NADPH. Maximal rates of .**omega**.-**hydroxylation** occurred at pH 8 and the rate increased in a sigmoidal manner with increasing concns. of palmitic acid. This .**omega**.-**hydroxylation** was inhibited by the classical **mixed function oxidase** inhibitors such as metal chelators (o-phenanthroline, 8-hydroxyquinoline, and .**alpha**.,.**alpha**.-dipyridyl), NaN3, and thiol reagents (N-ethylmaleimide and p-chloromercuribenzoate). As expected of a hydroxylase, involving cytochrome P450, the present o-hydroxylase was inhibited by CO and this enzyme system showed unusually high sensitivity to this inhibition; 10% CO caused inhibition and 30% CO completely inhibited the reaction. Another unusual feature was that the inhibition caused by any level of CO could not be reversed by light (420-460 nm).

TI Biosynthesis of cutin. .**omega**.-**Hydroxylation** of fatty acids by a microsomal **preparation** from germinating Vicia faba

AB .omega.-**Hydroxylation** of fatty acids, which is a key reaction in the biosynthesis of cutin and suberin, was demonstrated in a cell-free **prepn**. from a higher plant. A crude microsomal fraction (105,000-g pellet) from germinating embryonic shoots of V. faba catalyzed the conversion of palmitic acid to .omega.-hydroxypalmitic acid.

As the crude cell-free **prepn**. also catalyzes the formation of other hydroxy acids such as .**alpha**.- and .beta.-hydroxy acids, the .**omega**.-**hydroxylation** product was identified by gas chromatog. on a polyester column and reverse phase, high performance liq. chromatog., 2 techniques which were shown to resolve the positional isomers. Gas chromatog. anal. of the **dicarboxylic acid** obtained by CrO3 oxidn. of the enzymic product also confirmed the identity of the enzymic .**omega**.-**hydroxylation** product. This enzymic **hydroxylation** required O and NADPH, but substitution of NADH resulted in nearly half the reaction rate obtained with NADPH. Maximal rates of .**omega**.-**hydroxylation** occurred at pH 8 and the rate increased in a sigmoidal manner with increasing concns. of palmitic acid. This .**omega**.-**hydroxylation** was inhibited by the classical **mixed function oxidase** inhibitors such as metal chelators (o-phenanthroline, 8-hydroxyquinoline, and .**alpha**.,.**alpha**.-dipyridyl), NaN3, and thiol reagents (N-ethylmaleimide and p-chloromercuribenzoate). As expected of a hydroxylase, involving cytochrome P450, the present o-hydroxylase was inhibited by CO and this enzyme system showed unusually

high sensitivity to this inhibition; 10% CO caused inhibition and 30% CO completely inhibited the reaction. Another unusual feature was that the inhibition caused by any level of CO could not be reversed by light (420-460 nm).

ST **omega hydroxylation** fatty acid Vicia

IT Fatty acids, biological studies
RL: RCT (Reactant)
(.**omega.-hydroxylation** of, by microsome from broad bean)

IT Hydroxylation
(omega, of fatty acids by microsomal **prepn.** from Vicia faba)

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=> d full history

     (FILE 'HOME' ENTERED AT 08:53:03 ON 10 MAY 2001)

     FILE 'CAPLUS' ENTERED AT 08:53:11 ON 10 MAY 2001
                E .BETA.-OXIDN.-BLOCKED/CT
                E E2
                E E3+ALL
                E .BETA.-OXIDATION/CT
                E E3+ALL

     FILE 'REGISTRY' ENTERED AT 09:37:48 ON 10 MAY 2001
L1              1 SEA ABB=ON  PLU=ON  9038-14-6/RN
                  D
L2              1 SEA ABB=ON  PLU=ON  9023-03-4/RN
                  D

     FILE 'CAOLD, CAPLUS, CROPU, DGENE, DPCI, ENCOMPPAT, ENCOMPPAT2,
     EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE,
     PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2,
     USPATFULL, WPIDS' ENTERED AT 09:39:31 ON 10 MAY 2001

     FILE 'REGISTRY' ENTERED AT 09:39:57 ON 10 MAY 2001
                SET SMARTSELECT ON
L3              SEL PLU=ON  L1 1- CHEM :      26 TERMS
                SET SMARTSELECT OFF

     FILE 'CAOLD, CAPLUS, CROPU, DGENE, DPCI, ENCOMPPAT, ENCOMPPAT2,
     EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE,
     PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2,
     USPATFULL, WPIDS' ENTERED AT 09:40:22 ON 10 MAY 2001

     FILE 'REGISTRY' ENTERED AT 09:40:25 ON 10 MAY 2001
                SET SMARTSELECT ON
L4              SEL PLU=ON  L2 1- CHEM :      16 TERMS
                SET SMARTSELECT OFF

     FILE 'CAOLD, CAPLUS, CROPU, DGENE, DPCI, ENCOMPPAT, ENCOMPPAT2,
     EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE,
     PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2,
     USPATFULL, WPIDS' ENTERED AT 09:40:33 ON 10 MAY 2001
L5          18788 SEA ABB=ON  PLU=ON  L3
L6           7868 SEA ABB=ON  PLU=ON  L4
L7          25412 SEA ABB=ON  PLU=ON  L5 OR L6
L8         830900 SEA ABB=ON  PLU=ON  DICARBOXYLIC ACID# OR (CARBOXYLIC ACIDS
                  (L) DICARBOXYLIC) OR CARBOXYLIC ACID# OR MONOCARBOXYLIC ACID#
L9            573 SEA ABB=ON  PLU=ON  L7 AND L8
L10           361 SEA ABB=ON  PLU=ON  L9 AND (PREPAR? OR SYNTHES? OR MAK? OR
                  PREP/RL)
L11         11119 SEA ABB=ON  PLU=ON  (HYDROXYLATION (L) .OMEGA.-HYDROXYLATION)
                  OR (HYDROXYLATION (L) ALKANE#) OR (.ALPHA.-HYDROXYLATION) OR
                  (HYDROXYLATION (L) .ALPHA.)
L12           76 SEA ABB=ON  PLU=ON  L11 AND L10
L13           74 DUP REM L12 (2 DUPLICATES REMOVED)
L14         1066 SEA ABB=ON  PLU=ON  CANDIDA MALTOSA OR CANDIDA CLOACAE OR
                  CANDIDA NOVELLUS OR CANDIDA SUBTROPICALIS
L15            7 SEA ABB=ON  PLU=ON  L14 AND L10
L16            6 DUP REM L15 (1 DUPLICATE REMOVED)
                  D IBIB AB 1-6
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D IBIB AB 1
D IBIB AB 1-6

=> d ibib ab 1-6

L16 ANSWER 1 OF 6 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 2000065061 PCTFULL EW 200044 ED 20001124
TITLE (ENGLISH): NUCLEIC ACID SEQUENCES FROM CANDIDA YEASTS WHICH CODE
CYTOCHROME B5 POLYPEPTIDES
TITLE (FRENCH): SEQUENCES D'ACIDE NUCLEIQUE ISSUES DE LEVURES DE CANDIDA ,
CODANT DES POLYPEPTIDES B5 CYTOCHROMES
TITLE (GERMAN): NUKLEINSAeURE-SEQUENZEN AUS CANDIDA HEFEN, DIE CYTOCHROM
B5-POLYPEPTIDE KODIEREN
INVENTOR(S): SCHUNCK, Wolf-Hagen; CHERNOGOLOV, Alexei
PATENT ASSIGNEE(S): MAX-DELBRUeCK-CENTRUM FUeR MOLEKULARE MEDIZIN
LANGUAGE OF PUBL.: German
LANGUAGE OF FILING: German
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000065061	A2	20001102

DESIGNATED STATES: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-DE1246 20000418
PRIORITY (ORIGINAL): DE 1999-199 18 763.0 19990424

ABEN The invention relates to nucleic acid sequences from Candida yeasts, preferably from **Candida maltosa** , which code
cytochrome b5 polypeptides, as well as to the corresponding cytochrome b5 polypeptides and their use for increasing the activity of cytochrome P450 systems, especially for stimulating the activity of alkane-hydroxylating and fatty acid-hydroxylating cytochrome P450 systems during the production of long-chained **dicarboxylic acids** (#ge#C10).

ABFR L'invention concerne des sequences d'acide nucleique issues de levures de Candida , de preference de **Candida maltosa** ,
qui codent des polypeptides b5 cytochromes. L'invention concerne egalement les polypeptides b5 cytochromes correspondants et leur utilisation pour augmenter l'activite de systemes P450 cytochromes, notamment pour stimuler l'activite de systemes P450 cytochromes a effet hydroxylant de l'alcane et de l'acide gras lors de la **preparation** d'acides dicarboxyliques a chaine longue (#ge#C10).

ABDE Die Erfindung betrifft Nukleinsaeure-Sequenzen aus Candida Hefen vorzugsweise aus **Candida maltosa** , die Cytochrom b5-
Polypeptide kodieren sowie die entsprechenden Cytochrom b5-Polypeptide und ihre Verwendung zur Erhoehung der Aktivitaet von Cytochrom P450 Systemen, insbesondere zur Stimulierung der Aktivitaet Alkan- und Fettsaeure-hydroxylierender Cytochrom P450 Systeme bei der Produktion langkettiger Dicarbonsaeuren (#ge#C10).

L16 ANSWER 2 OF 6 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 2000034473 PCTFULL EW 200024 ED 20000712
TITLE (ENGLISH): SEVEN TRANSMEMBRANE DOMAIN RECEPTOR ZSIG56
TITLE (FRENCH): DOMAINE TRANSMEMBRANAIRE 7 ZSIG56
INVENTOR(S): SHEPPARD, Paul, O.; ELLSWORTH, Jeff, L.
PATENT ASSIGNEE(S): ZYMOGENETICS, INC.
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000034473	A2	20000615

DESIGNATED STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-US28492 19991202
PRIORITY (ORIGINAL): US 1998-09/208691 19981210
ABEN The present invention relates to polynucleotide and polypeptide molecules for a seven transmembrane domain receptor designated zsig56. The polypeptides, and polynucleotides encoding them are useful treating pathological conditions in such diverse tissue, as kidney, thyroid, gastrointestinal, CSN and reproductive. Such conditions include hypertension, hyper- and hypothyroidism, neurotransmission, gastrointestinal motility, inflammation and reproduction. The present invention also includes antibodies to the zsig56 polypeptides.
ABFR L'invention concerne des molecules polynucleotidiques et polypeptidiques pour un recepteur du domaine transmembranaire 7 appele zsig56. Les polypeptides et les polynucleotides codant pour eux conviennent pour le traitement d'etats pathologiques de tissus aussi divers que les reins, la glande thyroide, le tube digestif, le systeme nerveux central et l'appareil genital. Lesdits etats pathologiques concernent l'hypertension, l'hyperthyroidie, l'hypothyroidie, la neurotransmission, le transit intestinal, l'inflammation et la reproduction. L'invention concerne egalement des anticorps diriges contre les polypeptides zsig56.

L16 ANSWER 3 OF 6 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 2000020566 PCTFULL EW 200015 ED 20000503
TITLE (ENGLISH): CYTOCHROME P450 **MONOOXYGENASE** AND NADPH CYTOCHROME P450
OXIDOREDUCTASE GENES AND PROTEINS RELATED TO THE OMEGA
HYDROXYLASE
COMPLEX OF CANDIDA TROPICALIS AND METHODS RELATING THERETO
TITLE (FRENCH): GENES DE LA **MONOOXYGENASE** DU CYTOCHROME P450 ET DE
L'OXYDOREDUCTASE NADPH DU CYTOCHROME P450 ET PROTEINES
ASSOCIEES AU
COMPLEXE DE L'OMEGA HYDROXYLASE DE CANDIDA TROPICALIS ET PROCEDES ASSOCIES
INVENTOR(S): WILSON, C., Ron; CRAFT, David, L.; EIRICH, L., Dudley;

ESHOO, Mark; MADDURI, Krishna, M.; CORNETT, Cathy, A.;
BRENNER, Alfred, A.; TANG, Maria; LOPER, John, C.; GLEESON, Martin

PATENT ASSIGNEE(S): HENKEL CORPORATION
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000020566	A2	20000413

DESIGNATED STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:	WO 1999-US20797	19990910
PRIORITY (ORIGINAL):	US 1998-60/103099	19981005
	US 1999-	19990310

ABEN Novel genes have been isolated which encode cytochrome P450 and NADPH reductase enzyme of the #ohgr#-hydroxylase complex of C. tropicalis 20336. Vectors including these genes, transfected host cells and transformed host cells are provided. Methods of producing of cytochrome P450 and NADPH reductase enzymes are also provided which involve transforming a host cell with a gene encoding these enzymes and culturing the cells. Methods of increasing the production of a **dicarboxylic acid** and methods of increasing production of the aforementioned enzymes are also provided which involve increasing in the host cell the number of genes encoding these enzymes. A method for discriminating members of a gene family by quantifying the expression of genes is also provided.

ABFR La presente invention conçerne des genes isoles qui codent pour des enzymes du cytochrome P450 et de reductase de NADPH du complexe #ohgr#-hydroxylase de C. tropicalis 20336. L'invention concerne aussi des vecteurs contenant ces genes, des cellules hotes transfectees ainsi que des cellules hotes transformees. Sont aussi decrits des procedes de production des enzymes du cytochrome P450 et de reductase de NADPH qui consistent a transformer une cellule hote a l'aide d'un gene qui code pour ces enzymes et a cultiver les cellules. L'invention concerne aussi des procedes d'augmentation de la production d'un acide dicarboxylique, des procedes d'augmentation de la production des enzymes mentionnees ci-dessus qui consistent a augmenter le nombre de genes qui codent pour ces enzymes dans les cellules hotes, ainsi qu'une methode destinee a distinguer des elements d'une famille de genes en quantifiant l'expression des genes.

L16 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
ACCESSION NUMBER: 1999:77701 CAPLUS
DOCUMENT NUMBER: 130:138397
TITLE: Yeasts with elevated cytochrome P450 levels and their use in the manufacture of monoterminal and diterminal aliphatic carboxylates from alkanes
INVENTOR(S): Fallon, Robert D.; Payne, Mark S.; Picataggio, Stephen K.; Wu, Shijun

PATENT ASSIGNEE(S): E.I. Du Pont De Nemours and Company, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9904014	A2	19990128	WO 1998-US14935	19980720
WO 9904014	A3	19990520		
W: AU, CA, IL, JP, NZ, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9884982	A1	19990210	AU 1998-84982	19980720
EP 1003881	A2	20000531	EP 1998-935806	19980720
R: DE, DK, ES, FR, GB, IT, NL, SE, IE				

PRIORITY APPLN. INFO.: US 1997-53215 P 19970721
WO 1998-US14935 W 19980720

AB Strains of Pichia pastoris and **Candida maltosa** that have increased cytochrome P 450 activity or lack the .beta.-oxidn. pathway that can be used to convert c6-C22 alkanes to monoterminal and diterminal **carboxylic acids** are described. Expression constructs carrying cytochrome P 450 genes under the control of powerful inducible promoters (AOX1, PGK) were constructed by std. methods and introduced into P. pastoris or C. maltosa to give novel or increased P 450 activities. Disruption of .beta.-oxidn. in C. maltosa was achieved by insertional inactivation of the POX4 gene. A strain of C. maltosa cultured in a complete medium that was supplemented with dodecane 20 g/L when glucose was almost completely depleted was able to generate dodecanedioic acid at 3.4 g/h for 51 h.

L16 ANSWER 5 OF 6 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998055612 PCTFULL
TITLE (ENGLISH): NEUROKININ B PRECURSORS
TITLE (FRENCH): PRECURSEURS DE NEUROKININE B
INVENTOR(S): SHEPPARD, Paul, O.
PATENT ASSIGNEE(S): ZYMOGENETICS, INC.
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9855612	A1	19981210

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1998-US10842 19980528
PRIORITY (ORIGINAL): US 1997-60/048290 19970602

ABEN The present invention relates to zneurok1 polypeptides and polynucleotides encoding the same. These polypeptides are novel members of a family of proteins that are precursors of neurokinin B, a ten amino

acid moiety of biological significance. The polypeptides, and polynucleotides encoding them, are useful in the study of prohormone convertase function and neurokinin receptors. The present invention also includes antibodies to the zneurok1 polypeptides.

ABFR Cette invention concerne des polypeptides zneurok1 ainsi que des polynucleotides codant ces derniers. Ces polypeptides consistent en de nouveaux membres d'une famille de proteines qui sont des precurseurs de neurokinine B, un fragment de l'acide amine dix jouant un role biologique important. Ces polypeptides, ainsi que les polynucleotides qui les codent, sont utiles lors de l'etude de la fonction de convertase de prohormone, ainsi que des recepteurs de neurokinine. Cette invention concerne egalement des anticorps diriges contre les polypeptides zneurok1.

L16 ANSWER 6 OF 6 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1996027678 PCTFULL
TITLE (ENGLISH): PROCESS FOR HYDROXYLATING LONG-CHAIN ALKANES, FATTY ACIDS AND
OTHER ALKYL COMPOUNDS
TITLE (FRENCH): PROCEDE D'HYDROXYLATION D'ALCANES A LONGUE CHAINE, D'ACIDES GRAS
ET D'AUTRES COMPOSES ALKYLE
INVENTOR(S): ZIMMER, Thomas; KAMINSKI, Kristina; SCHUNCK, Wolf-Hagen; KAeRGEL, Eva; SCHELLER, Ulrich; MAUERSBERGER, Stephan
PATENT ASSIGNEE(S): MAX-DELBRUeCK-CENTRUM FUeR MOLEKULARE MEDIZIN; ZIMMER,
Thomas; KAMINSKI, Kristina; SCHUNCK, Wolf-Hagen; KAeRGEL, Eva; SCHELLER, Ulrich; MAUERSBERGER, Stephan
LANGUAGE OF PUBL.: German
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9627678	A1	19960912

DESIGNATED STATES: JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1996-DE410 19960301
PRIORITY (ORIGINAL): DE 1995-195 07 546.3 19950303

ABEN A microbial hydroxylation process is disclosed for selectively oxidising regions of long-chain alkanes, fatty acids and other alkyl compounds. The process should be easy to carry out and produce good yields of oxidation products, in particular hydroxylated fatty acids and long-chain **dicarboxylic acids**. The object of the invention is to modify
yeast by genetic engineering so that when it is cultivated it expresses the required enzymes. The disclosed process is characterised in that the long-chain alkanes, fatty acids and other alkyl compounds are treated with **monooxygenase** systems that consist of cytochrom P450 and NADPOH
cytochrom P450 reductase, and the hydroxylation products are then separated. The **monooxygenase** systems are produced in the reaction
mixture by simultaneous expression of their components in yeast, preferably saccharomyces cerevisiae. The invention relates essentially to a vector for modifying saccharomyces by genetic engineering. On the basis of the structure Yep 51, the vector contains reductase cDNA between the restriction sites SalK and BamHI and a second expression cassette bound in the restriction site NruI. The expression cassette consists of the GAL10 promoter, the sequence that codes for cytochrom

P450 and the ADH1 terminator.

ABF L'invention concerne un procede d'hydroxylation microbienne qui sert a oxyder selectivement des regions d'alcanes a longue chaine, d'acides gras et d'autres composes alkyle. Le procede doit permettre d'obtenir de maniere aisee un bon rendement en produits d'oxydation, notamment des acides gras hydroxyles et des acides dicarboxyliques a longue chaine. L'invention a pour objet de modifier par genie genetique des levures de sorte qu'elles expriment les enzymes requises lorsqu'elles sont cultivees. Le procede se caracterise en ce que l'on traite les alcanes a longue chaine, les acides gras et les autres composes alkyle avec des systemes a **monooxygenase** constitues de cytochrome P450 et de NADPH-cytochrome P450-reductase, les produits d'hydroxylation etant ensuite isoles. Les systemes a **monooxygenase** sont produits dans le melange de reaction par expression simultanee de leurs composants dans des levures, de preference la saccharomyces cerevisiae. L'invention porte essentiellement sur un vecteur de modification par genie genetique de saccharomyces, qui sur la base de la structure fondamentale Yep 51 contient l'ADNc de la reductase entre les sites de restriction Sa1I et BamHI et une deuxieme cassette d'expression liee dans le site de restriction NruI et constituee du promoteur GAL10, de la sequence de codage de cytochrome P450 et du terminateur ADH1.

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=> d full history

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     FILE 'REGISTRY' ENTERED AT 11:17:52 ON 10 MAY 2001
L1             1 SEA ABB=ON  PLU=ON  9038-14-6/RN
                 D
L2             1 SEA ABB=ON  PLU=ON  9023-03-4/RN
                 D

     FILE 'HCAPLUS' ENTERED AT 11:18:36 ON 10 MAY 2001

     FILE 'REGISTRY' ENTERED AT 11:18:51 ON 10 MAY 2001
                 SET SMARTSELECT ON
L3               SEL PLU=ON  L1 1- CHEM :      26 TERMS
                 SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 11:18:52 ON 10 MAY 2001

     FILE 'REGISTRY' ENTERED AT 11:18:53 ON 10 MAY 2001
                 SET SMARTSELECT ON
L4               SEL PLU=ON  L2 1- CHEM :      16 TERMS
                 SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 11:18:54 ON 10 MAY 2001
L5           15271 SEA ABB=ON  PLU=ON  L3
L6            7478 SEA ABB=ON  PLU=ON  L4
L7           21584 SEA ABB=ON  PLU=ON  L5 OR L6
L8          188643 SEA ABB=ON  PLU=ON  DICARBOXYLIC ACID# OR (CARBOXYLIC ACIDS
                   (L) DICARBOXYLIC) OR CARBOXYLIC ACID# OR MONOCARBOXYLIC ACID#
L9            5883 SEA ABB=ON  PLU=ON  (HYDROXYLATION (L) .OMEGA.-HYDROXYLATION)
                   OR (HYDROXYLATION (L) ALKANE#) OR (.ALPHA.-HYDROXYLATION) OR
                   (HYDROXYLATION (L) .ALPHA.)
L10           1338 SEA ABB=ON  PLU=ON  PICHIA PASTORIS
L11              4 SEA ABB=ON  PLU=ON  L7 (L) L8 (L) L9
                 D IBIB AB 1-4
                 D IBIB AB HIT 1-4
L12              0 SEA ABB=ON  PLU=ON  L11 AND L10
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=> d ibib ab 1-4

L11 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:5685 HCAPLUS
DOCUMENT NUMBER: 118:5685
TITLE: Metabolic engineering of Candida tropicalis for the production of long-chain dicarboxylic acids
AUTHOR(S): Picataggio, Stephen; Rohrer, Tracy; Deanda, Kristine; Lanning, Dawn; Reynolds, Robert; Mielenz, Jonathan; Eirich, L. Dudley
CORPORATE SOURCE: Microb. Technol. Dep., Cognis Inc., Santa Rosa, CA, 95407, USA
SOURCE: Bio/Technology (1992), 10(8), 894-8
CODEN: BTCHDA; ISSN: 0733-222X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An industrial strain of the yeast C. tropicalis was engineered for the efficient prodn. of long-chain **dicarboxylic acids**, which are important raw materials for the chem. industry. By sequential disruption of the 4 genes encoding both isoenzymes of the acyl-CoA oxidase which catalyzes the first reaction in the .beta.-oxidn. pathway, **alkane** and fatty acid substrates were successfully redirected to the .omega.-oxidn. pathway. Consequently, the conversion efficiency and chem. selectivity of their terminal oxidn. to the corresponding **dicarboxylic acids** was improved to 100%. The specific productivity of the bioconversion was increased further by amplification of the **cytochrome P 450 monooxygenase** and NADPH-cytochrome reductase genes encoding the rate-limiting .omega.-hydroxylase in the .omega.-oxidn. pathway. The amplified strains demonstrated increased .omega.-hydroxylase activity and a 30% increase in productivity compared to the .beta.-oxidn.-blocked strain in fermns. The bioconversion is effective for the selective terminal oxidn. of both satd. and unsatd. linear aliph. substrates with C12-22 chain-lengths and also avoids the undesirable chain modifications assocd. with passage through the .beta.-oxidn. pathway, such as unsatn., **hydroxylation**, or chain shortening. It is now possible to efficiently produce a wide range of previously unavailable satd. and unsatd. **dicarboxylic acids** with a high degree of purity.

L11 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:220705 HCAPLUS
DOCUMENT NUMBER: 114:220705
TITLE: Microsomal oxidation of dodecylthioacetic acid (a 3-thia fatty acid) in rat liver
AUTHOR(S): Hvattum, Erlend; Bergseth, Steinar; Pedersen, Catharina N.; Bremer, Jon; Aarsland, Asle; Berge, Rolf K.
CORPORATE SOURCE: Inst. Med. Biochem., Univ. Oslo, Oslo, 0317, Norway
SOURCE: Biochem. Pharmacol. (1991), 41(6-7), 945-53
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB [1-14C]Dodecylthioacetic acid (DTA), a 3-thia fatty acid, is .omega.(.omega.-1)-hydroxylated and sulfur oxygenated at about equal rates in rat liver microsomes. In prolonged incubations DTA is converted to

.omega.-hydroxydodecylsulfoxyacetic acid. .**omega**.-**Hydroxylation** of DTA is catalyzed by cytochrome P450IVA1 (or a very closely related isoenzyme in the same gene family), the fatty acid .omega.-hydroxylating enzyme. It is absolutely dependent on NADPH and inhibited by CO, and lauric acid is a competing substrate. .**omega**.-**Hydroxylation** of DTA is increased by feeding tetradecylthioacetic acid (TTA), a 3-thia fatty acid, for 4 days to rats. .**omega**.-**Hydroxylation** of [1-14C] lauric acid is also induced by TTA and other 3-thia **carboxylic acids**. A close relationship was obsd. between induction of microsomal .**omega**.-**hydroxylation** of fatty acid and palmitoyl-CoA hydrolase activity. DTA is .omega.-hydroxylated at about the same rate as the physiol. substrate lauric acid. The sulfur oxygenation of DTA is catalyzed by liver microsomal **flavin-contg**. **monooxygenase** (FMO) (EC 1.14.13.8). It is dependent on either NADH or lNADPH. The Km value for NADH was .apprx.five times larger than the Km value for NADPH. It is inhibited by methimazole and not affected by CO. It is not induced by TTA.

L11 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:61628 HCAPLUS
DOCUMENT NUMBER: 102:61628
TITLE: Oxidative ether cleavage with p-nitroperbenzoic acid
AUTHOR(S): Schneider, Hans Joerg; Ahlhelm, Alfred; Mueller, Walter
CORPORATE SOURCE: Univ. Saarlandes, Saarbruecken, D-6600/11, Fed. Rep. Ger.
SOURCE: Chem. Ber. (1984), 117(11), 3297-302
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The reaction of p-nitroperbenzoic acid in CHCl3 with Me2CH(CH2)3OMe and (Me2CHCH2CH2)2O leads by selective attack at C-H bonds in the .**alpha**.-position to the ether oxygen to hemiacetals, which decomp. to aldehydes and alcs., yielding **carboxylic acids**. Secondary alkoxy groups, as in ethoxycyclohexane, furnish Baeyer-Villiger oxidn. products of initially formed ketones. Kinetic measurements with substituted benzyl Me ethers show a Hammett reaction const. .rho. = -0.9, which is in accord with the obsd. relatively small discrimination between secondary and tertiary C-H bonds. The results are compared with similar **hydroxylations** of **alkanes** and with **monooxygenase** reactions and point to oxenoid transition states. Radical reactions, as found with some **alkanes** are not obsd., which is shown by the small amts. of PhNO2 (.ltoreq.10%) formed during the reaction. 13C-NMR shifts of several ethers and oxidn. products are reported.

L11 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1977:498893 HCAPLUS
DOCUMENT NUMBER: 87:98893
TITLE: Biosynthesis of cutin. .omega.-Hydroxylation of fatty acids by a microsomal preparation from germinating Vicia faba
AUTHOR(S): Soliday, Charles L.; Kolattukudy, P. E.
CORPORATE SOURCE: Dep. Agric. Chem., Washington State Univ., Pullman, Wash., USA
SOURCE: Plant Physiol. (1977), 59(6), 1116-21
CODEN: PLPHAY
DOCUMENT TYPE: Journal

LANGUAGE: English

AB .omega.-**Hydroxylation** of fatty acids, which is a key reaction in the biosynthesis of cutin and suberin, was demonstrated in a cell-free prepn. from a higher plant. A crude microsomal fraction (105,000-g pellet) from germinating embryonic shoots of V. faba catalyzed the conversion of palmitic acid to .omega.-hydroxypalmitic acid. As the crude cell-free prepn. also catalyzes the formation of other hydroxy acids such as .**alpha**.- and .beta.-hydroxy acids, the .**omega**.-**hydroxylation** product was identified by gas chromatog. on a polyester column and reverse phase, high performance liq. chromatog., 2 techniques which were shown to resolve the positional isomers. Gas chromatog. anal. of the **dicarboxylic acid** obtained by CrO3 oxidn. of the enzymic product also confirmed the identity of the enzymic .**omega**.-**hydroxylation** product. This enzymic **hydroxylation** required O and NADPH, but substitution of NADH resulted in nearly half the reaction rate obtained with NADPH. Maximal rates of .**omega**.-**hydroxylation** occurred at pH 8 and the rate increased in a sigmoidal manner with increasing concns. of palmitic acid. This .**omega**.-**hydroxylation** was inhibited by the classical **mixed function oxidase** inhibitors such as metal chelators (o-phenanthroline, 8-hydroxyquinoline, and .**alpha**.,.**alpha**.-dipyridyl), NaN3, and thiol reagents (N-ethylmaleimide and p-chloromercuribenzoate). As expected of a hydroxylase, involving cytochrome P450, the present o-hydroxylase was inhibited by CO and this enzyme system showed unusually high sensitivity to this inhibition; 10% CO caused inhibition and 30% CO completely inhibited the reaction. Another unusual feature was that the inhibition caused by any level of CO could not be reversed by light (420-460 nm).

=> d ibib ab hit 1-4

L11 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1993:5685 HCAPLUS

DOCUMENT NUMBER: 118:5685

TITLE: Metabolic engineering of Candida tropicalis for the production of long-chain dicarboxylic acids

AUTHOR(S): Picataggio, Stephen; Rohrer, Tracy; Deanda, Kristine; Lanning, Dawn; Reynolds, Robert; Mielenz, Jonathan; Eirich, L. Dudley

CORPORATE SOURCE: Microb. Technol. Dep., Cognis Inc., Santa Rosa, CA, 95407, USA

SOURCE: Bio/Technology (1992), 10(8), 894-8
CODEN: BTCHDA; ISSN: 0733-222X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An industrial strain of the yeast C. tropicalis was engineered for the efficient prodn. of long-chain **dicarboxylic acids**, which are important raw materials for the chem. industry. By sequential disruption of the 4 genes encoding both isoenzymes of the acyl-CoA oxidase which catalyzes the first reaction in the .beta.-oxidn. pathway, **alkane** and fatty acid substrates were successfully redirected to the .omega.-oxidn. pathway. Consequently, the conversion efficiency and chem. selectivity of their terminal oxidn. to the corresponding **dicarboxylic acids** was improved to 100%. The specific productivity of the bioconversion was increased further by amplification of the **cytochrome P 450**

monooxygenase and NADPH-cytochrome reductase genes encoding the rate-limiting .omega.-hydroxylase in the .omega.-oxidn. pathway. The amplified strains demonstrated increased .omega.-hydroxylase activity and a 30% increase in productivity compared to the .beta.-oxidn.-blocked strain in fermns. The bioconversion is effective for the selective terminal oxidn. of both satd. and unsatd. linear aliph. substrates with C12-22 chain-lengths and also avoids the undesirable chain modifications assocd. with passage through the .beta.-oxidn. pathway, such as unsatn., **hydroxylation**, or chain shortening. It is now possible to efficiently produce a wide range of previously unavailable satd. and unsatd. **dicarboxylic acids** with a high degree of purity.

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L11 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:220705 HCAPLUS
DOCUMENT NUMBER: 114:220705
TITLE: Microsomal oxidation of dodecylthioacetic acid (a 3-thia fatty acid) in rat liver
AUTHOR(S): Hvattum, Erlend; Bergseth, Steinar; Pedersen, Catharina N.; Bremer, Jon; Aarsland, Asle; Berge, Rolf K.
CORPORATE SOURCE: Inst. Med. Biochem., Univ. Oslo, Oslo, 0317, Norway
SOURCE: Biochem. Pharmacol. (1991), 41(6-7), 945-53
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB [1-14C]Dodecylthioacetic acid (DTA), a 3-thia fatty acid, is .omega.(.omega.-1)-hydroxylated and sulfur oxygenated at about equal rates in rat liver microsomes. In prolonged incubations DTA is converted to .omega.-hydroxydodecylsulfoxyacetic acid. **.omega.-Hydroxylation** of DTA is catalyzed by cytochrome P450IVA1 (or a very closely related isoenzyme in the same gene family), the fatty acid .omega.-hydroxylating enzyme. It is absolutely dependent on NADPH and inhibited by CO, and lauric acid is a competing substrate. **.omega**

.-**Hydroxylation** of DTA is increased by feeding tetradecylthioacetic acid (TTA), a 3-thia fatty acid, for 4 days to rats. .**omega**.-**Hydroxylation** of [1-14C] lauric acid is also induced by TTA and other 3-thia **carboxylic acids**. A close relationship was obsd. between induction of microsomal .**omega**.-**hydroxylation** of fatty acid and palmitoyl-CoA hydrolase activity. DTA is .omega.-hydroxylated at about the same rate as the physiol. substrate lauric acid. The sulfur oxygenation of DTA is catalyzed by liver microsomal **flavin-contg**. **monooxygenase** (FMO) (EC 1.14.13.8). It is dependent on either NADH or lNADPH. The Km value for NADH was .apprx.five times larger than the Km value for NADPH. It is inhibited by methimazole and not affected by CO. It is not induced by TTA.

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L11 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:61628 HCAPLUS
DOCUMENT NUMBER: 102:61628
TITLE: Oxidative ether cleavage with p-nitroperbenzoic acid
AUTHOR(S): Schneider, Hans Joerg; Ahlhelm, Alfred; Mueller, Walter
CORPORATE SOURCE: Univ. Saarlandes, Saarbruecken, D-6600/11, Fed. Rep. Ger.
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AB The reaction of p-nitroperbenzoic acid in CHCl3 with Me2CH(CH2)3OMe and (Me2CHCH2CH2)2O leads by selective attack at C-H bonds in the .**alpha**.-position to the ether oxygen to hemiacetals, which decomp. to aldehydes and alcs., yielding **carboxylic acids**. Secondary alkoxy groups, as in ethoxycyclohexane, furnish Baeyer-Villiger oxidn. products of initially formed ketones. Kinetic measurements with substituted benzyl Me ethers show a Hammett reaction const. .rho. = -0.9, which is in accord with the obsd. relatively small discrimination between secondary and tertiary C-H bonds. The results are compared with similar **hydroxylations** of **alkanes** and with **monooxygenase**

reactions and point to oxenoid transition states. Radical reactions, as found with some **alkanes** are not obsd., which is shown by the small amts. of PhNO2 (.ltoreq.10%) formed during the reaction. 13C-NMR shifts of several ethers and oxidn. products are reported.

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L11 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1977:498893 HCAPLUS
DOCUMENT NUMBER: 87:98893
TITLE: Biosynthesis of cutin. .omega.-Hydroxylation of fatty acids by a microsomal preparation from germinating Vicia faba
AUTHOR(S): Soliday, Charles L.; Kolattukudy, P. E.
CORPORATE SOURCE: Dep. Agric. Chem., Washington State Univ., Pullman, Wash., USA
SOURCE: Plant Physiol. (1977), 59(6), 1116-21
CODEN: PLPHAY
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .**omega**.-**Hydroxylation** of fatty acids, which is a key reaction in the biosynthesis of cutin and suberin, was demonstrated in a cell-free prepn. from a higher plant. A crude microsomal fraction (105,000-g pellet) from germinating embryonic shoots of V. faba catalyzed the conversion of palmitic acid to .omega.-hydroxypalmitic acid. As the crude cell-free prepn. also catalyzes the formation of other hydroxy acids such as .**alpha**.- and .beta.-hydroxy acids, the .**omega**.-**hydroxylation** product was identified by gas chromatog. on a polyester column and reverse phase, high performance liq. chromatog., 2 techniques which were shown to resolve the positional isomers. Gas chromatog. anal. of the **dicarboxylic acid** obtained by CrO3 oxidn. of the enzymic product also confirmed the identity of the enzymic .**omega**.-**hydroxylation** product. This enzymic **hydroxylation** required O and NADPH, but substitution of NADH resulted in nearly half the reaction rate obtained with NADPH. Maximal rates of .**omega**.-**hydroxylation** occurred at pH 8 and the rate increased in a sigmoidal manner with increasing concns. of palmitic acid. This .**omega**.-**hydroxylation** was inhibited by the classical **mixed function oxidase** inhibitors such as metal chelators (o-phenanthroline, 8-hydroxyquinoline, and .**alpha**.,.**alpha**.-dipyridyl), NaN3, and thiol reagents (N-ethylmaleimide and p-chloromercuribenzoate). As expected of a hydroxylase, involving cytochrome P450, the present o-hydroxylase was inhibited by CO and this enzyme system showed unusually high sensitivity to this inhibition; 10% CO caused inhibition and 30% CO completely inhibited the reaction. Another unusual feature was that the

inhibition caused by any level of CO could not be reversed by light (420-460 nm).

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